



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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What's New in the Pediatric Guidelines (Last updated April 14, 2020; last reviewed April 14, 2020)

The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) has reviewed previous versions of the *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* and revised the text and references. Key updates are summarized below.

April 14, 2020

When to Initiate Therapy in Antiretroviral-Naive Children

- The Panel now recommends rapid initiation of antiretroviral therapy (ART) for **all** children, not just those aged <1 year. Rapid initiation is defined as initiating therapy immediately or within days of HIV diagnosis.
- Because the Panel no longer makes recommendations about when to initiate ART based on a child's age (either <1 year of age or ≥1 year of age), Table A has been deleted and the data that support rapid initiation have been grouped by outcome (i.e., survival and health benefits, neurodevelopmental benefits, immune benefits, and viral reservoirs and viral suppression). References have been updated to reflect recently published findings, and older references have been removed.
- The Panel acknowledges that, on a case-by-case basis, initiation of ART may be deferred based on a patient's clinical or psychosocial factors. The Panel highlights medical factors, including HIV signs and symptoms, that should be considered when clinicians, patients, and caregivers make collaborative decisions about whether to defer treatment.
- With the changes described above, the Treatment Recommendations section is no longer needed and has been deleted.

What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children

- Text and Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children have been updated following Food and Drug Administration (FDA) approval of cobicistat (COBI) for pediatric use.
- The Panel now recommends atazanavir (ATV) boosted with COBI (ATV/c) or darunavir (DRV) boosted with COBI (DRV/c) plus two nucleoside reverse transcriptase inhibitors as *Alternative* protease inhibitor-based initial regimens for children and adolescents aged ≥12 years with a sexual maturity rating of 1 to 3 who weigh ≥35 kg or ≥40 kg, respectively.
- Throughout the guidelines, the Panel refers to the Adult and Adolescent Antiretroviral Guidelines and the Perinatal Guidelines for guidance about the use of dolutegravir (DTG) and other antiretroviral (ARV) drugs in people of childbearing potential and those who are pregnant or who are trying to conceive.
 - Wording has been revised in accordance with updated recommendations about the use of DTG, and a link to the new [Appendix D. Dolutegravir Counseling Guide for Health Care Providers](#) in the Perinatal Guidelines has been inserted into several sections.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or HIV Infection

- The Panel has changed the term “empiric HIV therapy” to “presumptive HIV therapy” in this section and throughout the guidelines to be consistent with the terminology used by the World Health Organization. The Panel recommends presumptive HIV therapy for infants who are at a higher risk of perinatal HIV

acquisition. For clarity, the term “multidrug ARV prophylaxis” has been changed to “two-drug ARV prophylaxis.”

- Table 11. Neonatal Antiretroviral Management According to Risk of HIV Infection in the Newborn and Table 12. Antiretroviral Dosing Recommendations for Newborns have been revised to clarify the ARV regimens and the duration and dosing of ARV drugs that are used for presumptive HIV therapy.
- The two-drug regimen that was used in NICHD-HPTN 040/PACTG 1043 for infants who were at a higher risk of HIV acquisition is no longer included in Tables 11 and 12; this regimen is described in the text instead, see the [Two-Drug Antiretroviral Prophylaxis](#) section.

Special Considerations for Antiretroviral Therapy Use in Adolescents with HIV

- The Panel added a new subsection entitled Special Considerations for Adolescents with HIV Who Are Sexual Minorities with links to [Adolescents and Young Adults with HIV](#) and [Transgender People with HIV](#) in the Adult and Adolescent Antiretroviral Guidelines.

Management of Medication Toxicity or Intolerance

- [Table 15a. Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Central Nervous System Toxicity](#) includes updated information about neuropsychiatric symptoms and other central nervous system manifestations that are associated with the use of integrase strand transfer inhibitors. Information on bictegravir has also been added to the table.
- Information about the association between ARV drugs and weight gain has been added to [Table 15h](#), and the table has been renamed Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations—Lipodystrophies and Weight Gain.

Management of Children Receiving Antiretroviral Therapy

- The sections on [Modifying Antiretroviral Regimens in Children with Sustained Virologic Suppression on Antiretroviral Therapy](#) and [Recognizing and Managing Antiretroviral Treatment Failure](#) have been updated to incorporate the most recent ART options for pediatric patients based on new pediatric ARV drug approvals and Panel recommendations.

Appendix A: Pediatric Antiretroviral Drug Information

The drug sections and [Appendix A, Table 2](#) were updated to include new pediatric data and dosing and safety information, plus new drug formulations and fixed-dose combination (FDC) drugs. Significant changes include:

- In accordance with FDA approval, raltegravir (RAL) HD is now recommended for use in children and adolescents weighing ≥ 40 kg who are treatment naive or who are virologically suppressed on an initial dose of RAL 400 mg twice daily.
- Although lopinavir/ritonavir is not approved by the FDA for use in neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days, the Panel now provides some guidance for situations where no alternatives are available for neonates who have not met these age thresholds.
- The ATV, DRV, and COBI drug sections have been updated to reflect recent FDA approvals and updated Panel recommendations. COBI (Tybost) is now approved by the FDA for use with ATV in children and adolescents weighing ≥ 35 kg and for use with DRV in children and adolescents weighing ≥ 40 kg. The FDC tablet darunavir/cobicistat/emtricitabine/tenofovir alafenamide (DRV/c/FTC/TAF; Symtuza) is now approved by the FDA for use in children and adolescents weighing ≥ 40 kg. Although coformulated ATV/c (Evotaz) and DRV/c (Prezcobix) are not approved by the FDA for use in children, the Panel does recommend using these FDC tablets in pediatric patients weighing ≥ 35 kg or ≥ 40 kg, respectively, based on FDA approvals of the individual component drugs.

December 24, 2019

The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) has updated the three sections of the *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* that developed in collaboration with the Panel on Treatment of Pregnant Women.

Maternal HIV Testing and Identification of Perinatal HIV Exposure

In addition to recommendations for repeat HIV testing in the third trimester, repeat HIV testing at other times during pregnancy should be considered when clinically indicated. For example, repeat testing should be performed when a woman presents with symptoms that are suggestive of a sexually transmitted infection (STI), when a woman presents with a confirmed STI diagnosis, or when a woman presents with symptoms that are consistent with acute HIV infection.

Diagnosis of HIV Infection in Infants and Children

The Panel has added some guidance about when consultation with a clinical virologist may be indicated when the mother of an infant acquired HIV infection outside of the U.S. and has had repeated undetectable HIV RNA by standard testing.

Antiretroviral Management of Newborns with Perinatal HIV Exposure or Perinatal HIV

When considering the risk of perinatal HIV transmission and the selection of appropriate ARV drugs for newborns with perinatal HIV exposure, the Panel now defines maternal viral suppression as an HIV RNA level of <50 copies/mL.

A new subsection summarizes information about choosing between empiric HIV therapy and multidrug ARV prophylaxis for newborns with perinatal HIV exposure who are at a high risk of perinatal HIV transmission.

The Panel has also clarified that nevirapine (NVP) can be replaced with lopinavir/ritonavir when infants who are receiving empiric HIV therapy reach a postmenstrual age ≥ 42 weeks and a postnatal age ≥ 14 days; NVP can be replaced with RAL at any age.

September 12, 2019

The Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV (the Panel) revised several sections of the April 16, 2019 *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection* to update content and recommendations about the use of the antiretroviral drugs bictegravir/emtricitabine/tenofovir alafenamide (Biktarvy) and dolutegravir in children and adolescents. The updates are summarized below.

What to Start: Regimens Recommended for Initial Therapy of Antiretroviral-Naive Children

- Table 7. Antiretroviral Regimens Recommended for Initial Therapy for HIV Infection in Children, Figure 1, and the associated text now include new recommendations for the use of bictegravir and dolutegravir in children:
 - The fixed-dose combination (FDC) tablet Biktarvy is now a *Preferred* integrase strand transfer inhibitor (INSTI)-based regimen for adolescents aged ≥ 12 years and weighing ≥ 25 kg (**AI**) and an *Alternative* INSTI-based regimen for children aged ≥ 6 years and weighing ≥ 25 kg (**AI**).
 - Dolutegravir plus two nucleoside reverse transcriptase inhibitors is now an *Alternative* INSTI-based regimen for children aged ≥ 3 years and weighing ≥ 20 kg to < 25 kg (**AI***). It was previously recommended only for children weighing ≥ 25 kg. Data are limited on the efficacy and safety of

administering dolutegravir to children weighing ≥ 20 kg to < 25 kg and dolutegravir pharmacokinetics vary more among children in this weight group than among those weighing ≥ 25 kg.

- Table 8. Advantages and Disadvantages of Antiretroviral Components Recommended for Initial Therapy in Children now includes information about Biktarvy.

What Not to Start: Regimens Not Recommended for Initial Therapy of Antiretroviral-Naive Children

- Bictegravir was removed from this section following Food and Drug Administration (FDA) approval for the use of Biktarvy in children and adolescents weighing ≥ 25 kg.

Modifying Antiretroviral Regimens in Children with Sustained Virologic Suppression on Antiretroviral Therapy

- Table 16. Examples of Changes in Antiretroviral Regimen Components for Children with Sustained Virologic Suppression has been updated to reflect revised recommendations for the use of bictegravir and dolutegravir.

Appendix A: Pediatric Antiretroviral Drug Information

- Certain drug sections and [Tables 1](#) and [2](#) were updated to include new pediatric data and dosing information for bictegravir and dolutegravir, including a new FDC tablet.
 - Bictegravir, which is available only in the FDC tablet Biktarvy, is now approved by the FDA for use in children and adolescents weighing ≥ 25 kg.
 - Based on recent data, the dosing recommendations for dolutegravir have been revised to allow use in children weighing ≥ 20 kg, although dolutegravir is not approved by the FDA for use in children weighing < 30 kg. A new table in this section compares FDA, European Medicines Agency (EMA), World Health Organization (WHO), and Panel dosing recommendations for dolutegravir. Dolutegravir/lamivudine (Dovato), a new FDC tablet that has been approved for use in adults, was added to the Dolutegravir and Lamivudine sections and to Tables 1 and 2.
 - The Emtricitabine and Tenofovir Alafenamide sections have been updated to reflect changes in the dosing recommendations for FDC tablets that contain bictegravir or dolutegravir.